Access DB# 78491

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Kathleen Kerr Examiner #: 77468 Date: 10/22/02
Art Unit: 1652 Phone Number 305-1229 Serial Number: 09/768979
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. mes

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): see attached

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please do a structure search of the compound of claim 107.

If no art before 1/24/00, please search for generic methotrexate —— dexamethasone compounds Dex-Y-Mtx (where Y is ∅ or anything)

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Shep Preuss	NA Sequence (#) _____	STN _____
Searcher Phone #: 308-4499	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: 10/24/02	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other (specify) _____

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FILE COVERS 1907 - 26 Oct 2002 VOL 137 ISS 18
FILE LAST UPDATED: 25 Oct 2002 (20021025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L13                 STR
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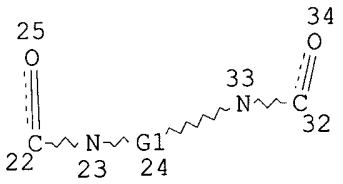

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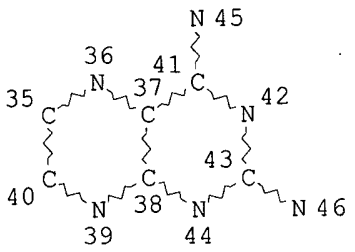

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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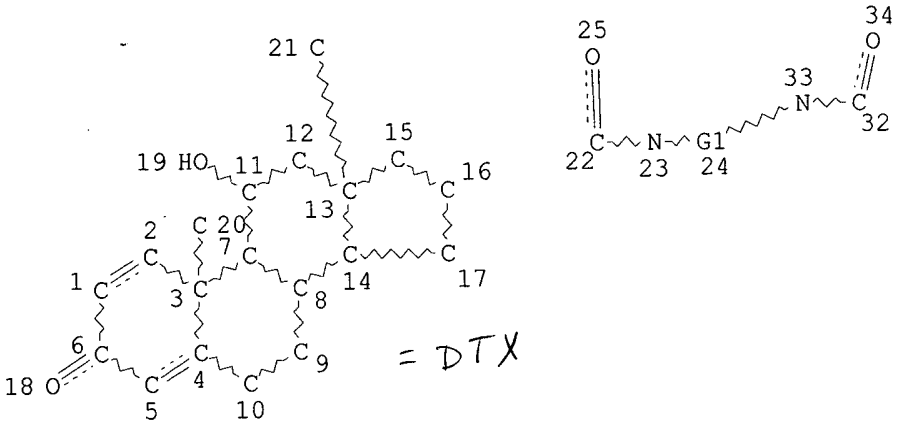
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L15 STR



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STEREO ATTRIBUTES: NONE
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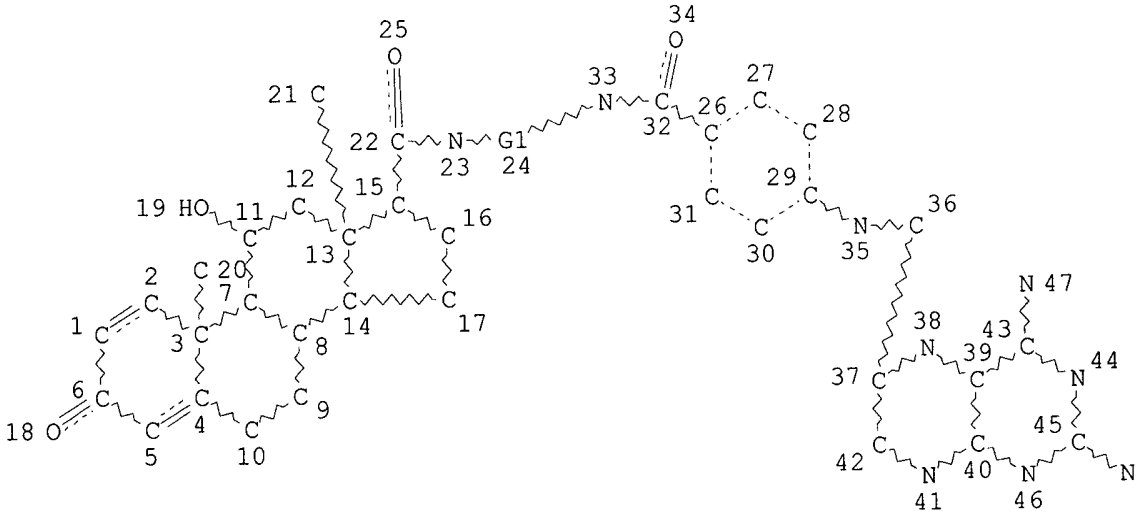

Page 1-A

48

Page 1-B
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DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE
L20 2 SEA FILE=REGISTRY SUB=L18 SSS FUL L19
L21 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L20

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=> d ibib abs hitrn l21 1-2

L21 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:31914 HCAPLUS
DOCUMENT NUMBER: 136:98820
TITLE: Yeast three-hybrid system for in vivo drug screening and enzyme evolution using chemical inducers of dimerization
INVENTOR(S): Cornish, Virginia W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 490,320.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002004202	A1	20020110	US 2001-768479	20010124
PRIORITY APPLN. INFO.:			US 2000-490320 A2	20000124

AB The disclosed invention relates to the evolution of enzymes in vivo, and drug screening in vivo through the use of chem. inducers of protein dimerization. The subject invention provides a compd. having the formula: H1--X--B-Y--H2 wherein each of H1 and H2 may be the same or different and capable of binding to a receptor which is the same or different; wherein each of X and Y may be present or absent and if present, each may be the same or different spacer moiety; and wherein B is an enzyme cleavable moiety. This invention also provides a method of screening proteins for the ability to catalyze bond cleavage or bond formation, comprising the steps of: (a) providing a cell that expresses a pair of fusion proteins which upon dimerization change a cellular readout; (b) providing the compd. of the invention which dimerizes the pair of fusion proteins, said compd. comprising two portions coupled by a bond that is cleavable or formed by the protein to be screened; and (c) screening for the cellular readout, wherein a change the cellular readout indicates catalysis of bond cleavage or bond formation by the protein to be screened. However, it has not heretofore been suggested to use small mol. induced protein dimerization to screen for catalysis in vivo., and specifically, it has not been suggested to use an enzyme cleavable moiety to link two mols. to dimerize proteins. This invention provides proteins de novo with prescribed binding and catalytic properties and permits screening cDNA libraries based on biochem. function. Practically, we believe that powerful screens in combination with existing randomization techniques will make it possible to take an existing protein fold and evolve it into an enzyme with a new function generating useful catalysts for the pharmaceutical and chem. industries. Since the screen is done in vivo and in both prokaryotes and eukaryotes, the methodol. can be applied to functional genomics and drug discovery. A new chem. inducer of

dimerization (CID) was recently developed in Professor Cornish's lab, which uses a heterodimer of methotrexate (MTX) and dexamethasone (DEX) which, when placed in the yeast three-hybrid system, reconstitutes transcription of the lacZ gene. The effects of altering the structure of the DEX-MTX CID and the protein chimeras in the three-hybrid assay were investigated. It was obsd. that all DEX-MTX CIDs, except the DEX-MTX CID with the shortest chem. linker, showed the ability to induce .beta.-galactosidase levels at levels 400% above strains possessing no CID. The DEX-MTX CIDs showed little or no increase in .beta.-galactosidase levels above background levels in strains where dihydrofolate reductase (DHFR) from E. coli was replaced by DHFR from murine. The three-hybrid system did show some directional preference to the way in which the receptors where fused to the DNA binding domain and the activation domain. These studies have led to a better understanding of the factors that are important in activating transcription in the DEX-MTX yeast three-hybrid system.

IT **389085-38-5**
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(yeast three-hybrid system for in vivo drug screening and enzyme evolution using chem. inducers of dimerization)

L21 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:545747 HCAPLUS
DOCUMENT NUMBER: 135:133932
TITLE: An in vivo screen using chemical inducers of dimerization
INVENTOR(S): Cornish, Virginia W.
PATENT ASSIGNEE(S): The Trustees of Columbia University in the City of New York, USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053355	A1	20010726	WO 2001-US2285	20010124

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-490320 A 20000124

AB The subject of the invention provides a compd. having the formula: H1-X-B-Y-H2, wherein each of H1 and H2 may be the same or different and capable of binding to a receptor which is the same or different; wherein each of X and Y may be present or absent and if present, each may be the same or different spacer moiety; and wherein B is an enzyme cleavable moiety. Said compds. can be called chem. inducers of dimerization. This invention also provides a method of screening proteins for the ability to catalyze bond cleavage.

IT **351419-40-4**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(compds. comprising receptor-binding moiety, spacer and enzyme cleavable moiety for screening drugs and proteins capable of catalyze bond cleavage)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> fil caold
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L22 0 L20

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 OCT 2002 HIGHEST RN 466118-13-8
DICTIONARY FILE UPDATES: 25 OCT 2002 HIGHEST RN 466118-13-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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=> d ide can l20 1-2

L20 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 389085-38-5 REGISTRY
CN Androsta-1,4-diene-17-carboxamide, N-[5-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]pentyl]-9-fluoro-11,17-dihydroxy-3-oxo-, (11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)
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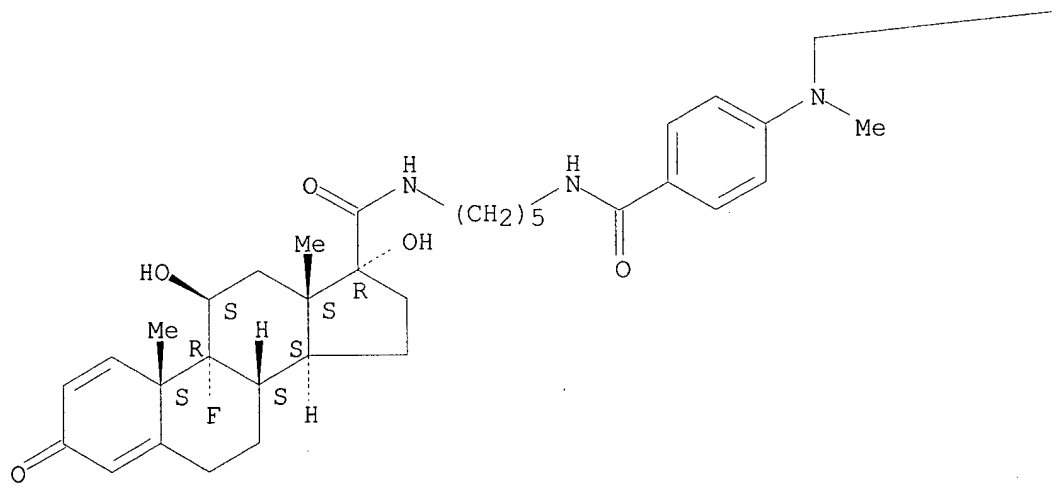
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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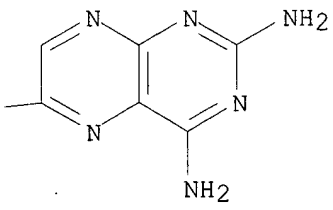


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

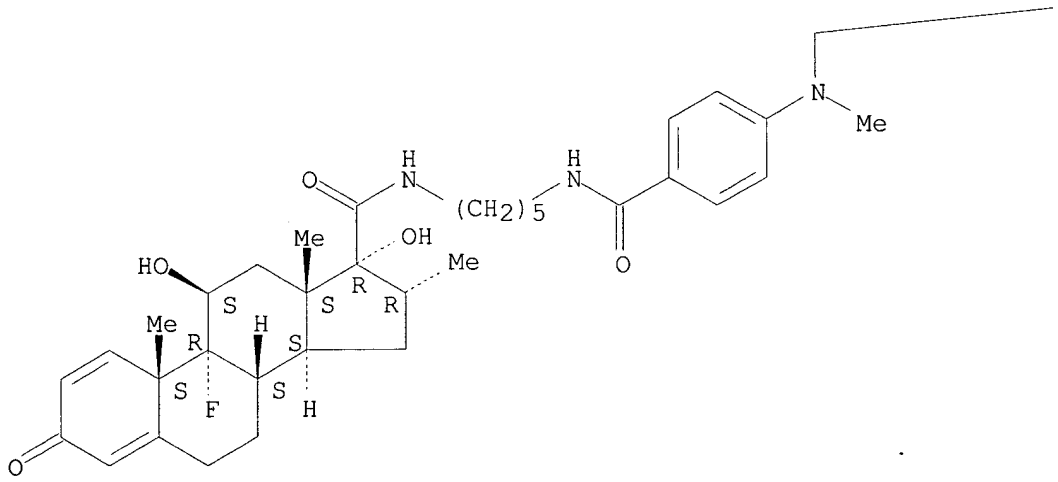
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:98820

L20 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 351419-40-4 REGISTRY
CN Androsta-1,4-diene-17-carboxamide, N-[5-[[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]amino]pentyl]-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11.beta.,16.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H52 F N9 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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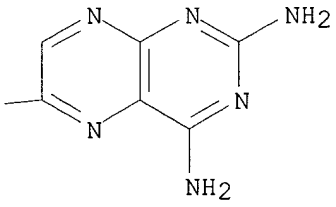

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:133932